

BRIEF COMMUNICATION



The role of teprotumumab in chronic, clinically active thyroid eye disease

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Thyroid eye disease (TED) is a chronic inflammatory condition that can lead to permanent disfigurement, disability, and vision loss. It is traditionally believed that TED is a self-limited disease that presents with an initial inflammatory stage followed by quiescent fibrotic changes. However, emerging data suggests that chronic TED may have more disease activity than previously thought, with persistently increased insulin-like growth factor-1 expression [1]. Unfortunately, few treatments have been studied in chronic, clinically active TED patients. Recent reports have shown that teprotumumab (Horizon Therapeutics, Dublin, IRL), a medication approved in the United States based on studies in acute, clinically active TED, may also be effective at reducing proptosis in chronic, clinically inactive TED [2–4]. A recent presentation suggested clinical improvement following initiation of teprotumumab in chronic, clinically active TED patients but no long term follow up data was described [5]. No publications to date discuss the use of teprotumumab in chronic, clinically active TED. Additionally, it is not known how prior treatments such as orbital radiation, decompression, and tocilizumab impact teprotumumab's efficacy. This case series describes the effect of teprotumumab in 6 patients with chronic, clinically active TED who have undergone prior medical and surgical treatments.

At a single centre academic institution, 6 patients presenting, on average, 10.4 years after being diagnosed with TED (range 1.2–29.6 years) were treated with teprotumumab (Table 1). Five out of 6 of these patients had completed a series of 8 infusions and 1

patient has received 6 out of a planned total of 8 infusions. By most recent follow up an average of 2.5 months after treatment completion, Clinical Activity Score (CAS) decreased by 1.5 (SD 3.0) and proptosis of the study orbit (orbit with greater proptosis prior to treatment) reduced by 3.8 mm (SD 2.1 mm).

The clinical response to treatment was variable [4, 5]. Patient 2, who had a 30-year history of TED with prior steroids, decompression, orbital radiation, and bilateral upper and left lower eyelid retraction repair, demonstrated a decrease in proptosis by 3 mm in the study orbit, but a stable CAS of 3. Her thyroid stimulating immunoglobulin decreased from 12.20 IU/L prior to treatment to 4.4 IU/L 3 months after treatment completion, suggesting a sustained immunologic response. In addition, despite scarring associated with prior eyelid procedures, she displayed stable improvement in eyelid retraction post-treatment (Fig. 1).

In contrast, Patient 3, who had an 8-year history of TED treated with steroids, decompression, and tocilizumab demonstrated an initial post treatment decrease in proptosis, reduction in CAS from 5 to 2, and improved eyelid position. However, 3 months after treatment, despite stable improvement in proptosis, her CAS increased to 7, and her eyelid retraction recurred.

This case series demonstrates that teprotumumab can be beneficial in chronic, clinically active TED patients who have had previous corticosteroid, tocilizumab, radiation, or surgery. Expanding treatment options for chronic, clinically active TED patients is important as no studies have been published in this population.

Table 1. Patient demographics and prior TED treatments with Baseline, Mid*, and Post treatment CAS scores and study orbit proptosis measurements.

Demographics				Prior treatments				CAS				Proptosis (mm)						
Patient	Age (yrs)	Sex	Duration (yrs)	# of Infusions	IV Steroids	Radiation	Decompression	Tocilizumab	Base-line	Mid*	Post (0 months)	Post (3 months)	Post (6 months)	Base-line	Mid*	Post (0 months)	Post (3 months)	Post (6 months)
1	58	F	7.6	8	Y	Y	N	N	4	3	2	N/A	N/A	30	28	26	N/A	N/A
2	74	F	29.6	8	Y	Y	Y	N	3	N/A	2	2	3	29	28	27	27	28
3	30	F	7.6	8	Y	N	Y	Y	5	4	2	7	N/A	32	30	28.5	27.5	N/A
4	67	F	11.6	6	N	N	Y	N	4	3	N/A	N/A	N/A	17	15	N/A	N/A	N/A
5	49	F	5.1	8	N	N	N	N	9	3	4	2	N/A	32	26	26	25	N/A
6	43	M	1.2	8	N	N	N	N	6	3	4	3	5	30.5	29	27	26	26

*"Mid" denotes exam findings the day of to 3 weeks after infusion number 4.

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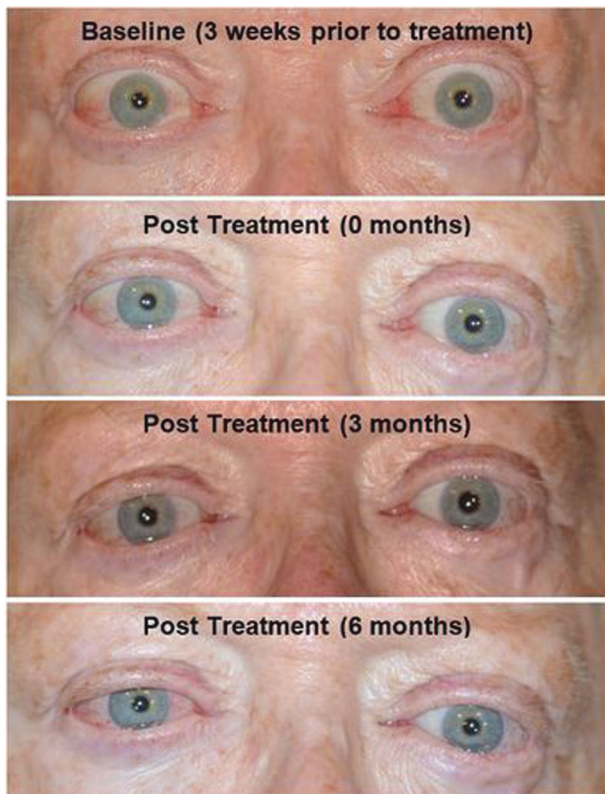


Fig. 1 External photographs of Patient 2. The patient had a nearly 30-year history of TED with prior steroids, decompression, orbital radiation, and bilateral upper and left lower eyelid retraction repairs, showing significant and sustained improvement in proptosis and eyelid retraction following teprotumumab.

Going forward, prospective studies are needed to evaluate treatment efficacy and elucidate the impact of prior treatments on patient outcomes and dosing requirements.

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AUTHOR CONTRIBUTIONS

CYY was responsible for extracting and analyzing data, interpreting the results, creating the figures, and writing the report. BAS contributed to interpreting the results, formatting the table, and editing the manuscript. CMP assisted with designing the review protocol, interpreting results, and editing the manuscript. EMS oversaw the review protocol design, data collection and screening, interpreting results, updating the reference list, and editing of the manuscript.

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EMS is a Consultant/Advisor for Horizon Therapeutics. The other authors have no financial or other conflicts of interests to disclose.

CONSENT FOR PUBLICATION

Consent to publish patient images has been obtained from the patient in writing.

ADDITIONAL INFORMATION

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